REMARKS

Claims 1-17 are pending in the instant application. Claims 6, 10-14, 16 and 17 have been withdrawn from consideration by the Examiner and subsequently canceled without prejudice by Applicants in this amendment. Claims 1-5, 7-9 and 15 have been rejected. Claims 1 and 15 have been amended. New claims 18 and 28 have been added. Support for these amendments is provided in the specification at page 14, line 19 through page 16, line 32, page 32, line 28 through page 33, line 15, Example 1 and in claim 1. Thus no new matter is added by these amendments. Reconsideration is respectfully requested in light so these amendments and the following remarks.

I. Finality of Restriction Requirement

The Examiner has made final the Restriction Requirement mailed September 22, 2003. Thus, in an earnest effort to advance the prosecution of this case, Applicants have canceled without prejudice non-elected claims 6, 10-14, 16 and 17. In light of the finality of this Restriction Requirement, Applicants reserve the right to file a divisional application to the canceled subject matter.

II. Objection to Claims

Claims 1-5, 7-9 and 15 have been objected to as reciting non-elected subject matter. Accordingly, in an earnest effort to advance the prosecution of this case. Applicants have amended these claims to be drawn to the elected sequence, SEQ ID NO:51, encoding SEQ ID NO:174. Withdrawal of this objection is therefore respectfully requested.

III. Objection to the Specification

The specification has been objected to. In particular, the Examiner suggests that the underscore at page 75, line 15 in the phrase "yeast_mating factor" should be deleted.

Further, the Examiner suggests that the embedded hyperlinks and/or other forms of browser executable code in the specification must be deleted.

Further the Examiner suggests that the title is not descriptive.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the title of the application to be more descriptive. Further, Applicants have replaced the underscore in the phrase "yeast_mating factor" with an --α-- symbol in accordance with this well known term of art. Finally, Applicants have amended the specification to inactivate

any embedded hyperlinks and/or other forms of browser executable code in the specification. Amendments to correct inadvertent typographical errors noted in the specification during review for the above issues were also made.

No new matter is added by any of these amendments to the specification.

Withdrawal of all objections to the specification is respectfully requested in light of these amendments.

IV. Rejection of Claims 1-5, 7-9 and 15 under 35 U.S.C. § 112, second paragraph

Claims 1-5, 7-9 and 15 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Examiner suggests that the phrase "selectively hybridizes" is not clear.

The claims are also suggested to be indefinite over claim 1(d) because the Examiner suggests that it is not clear as to how "a nucleic acid molecule having at least 60% sequence identity of (a) or (b) can encode an amino acid sequence of SEQ ID NO:174.

Thus, in an earnest effort to advance the prosecution of this case and in accordance with the Examiner's suggestion,

Applicants have amended the specification to recite hybridization conditions. Support for this amendment is provided in the specification at page 14, line 19 though page 16, line 32.

Further, Applicants have amended part (d) of claim 1 in accordance with teachings at page 32-33 of the specification to state that the nucleic acid molecule has at least 96% sequence identity over at least 200 nucleotides of the nucleic acid molecule of (a) or (b). Degeneracy of the genetic code is well understood by those skilled in the art and it is reasonable to expect a sequence with 96% identity or higher to a reference sequence to encode the same amino acid sequence as the reference sequence.

Thus, the claims as amended are clear and definite to one skilled in the art, thus meeting the requirements of 35 U.S.C. § 112, first paragraph, as set forth in MPEP § 2173.

Withdrawal of this rejection under 35 U.S.C. § 112, second paragraph is therefore respectfully requested.

V. Rejection of Claims 1-5, 7-9 and 15 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph

Claims 1-5, 7-9 and 15 have been rejected under 35 U.S.C. § 101 as the Examiner suggests that the claimed invention is not supported by either a substantial asserted utility, or a well

established utility. The Examiner has acknowledged Applicants' teaching that SEQ ID NO:51 has a "CLASP2CLASP1" profile. However, the Examiner suggests that there is no data or experimental analysis of SEQ ID NO:51 or the other claimed nucleic acids. Specifically, the Examiner suggests that the specification does not teach what tissues were used, whether diseases and normal samples were expressed and then compared against one another, how many patients the results stem from, relative expression levels in tissues and the source of the nucleic acids is (e.g. cell culture or tumor). The Examiner also suggests that specification is silent with respect to any potential nucleic acids that fall within claim 1(c) or 1(d). These claims had also been rejected under 35 U.S.C. § 112, first paragraph, for lack of utility, as the Examiner suggests that it would require undue experimentation for those skilled in the art to determine how to use the claimed invention.

Applicants respectfully traverse these rejections.

At the outset, Applicants respectfully disagree with the Examiner's suggestion that the specification is unclear with respect to the source of tissue of the nucleic acid sequence of SEQ ID NO:51 and the level of expression of SEQ ID NO:51 in cancer vs. normal tissue. The instant specification states at

page 117, lines 12 through 16 that to qualify as a CLASP 2 candidate, a gene must exhibit detectable expression in tumor tissues and undetectable expression in libraries from normal individuals and libraries from normal tissue obtained from diseased patients and the gene must exhibit further specificity for the tumor tissues of interest. Further at page 117, lines 22 through 26, it is taught that to qualify as a CLASP1 candidate, a gene must exhibit statistically significant expression in the tissue of interest compared to all other tissues. Thus, this teaching makes clear that the source of the tissue in which expression was observed was tumor tissue of interest and that this differential expression was compared to all other normal tissues. As made clear throughout the rest of the specification the tumor tissue of interest is lung cancer tissue. Further, teachings at page 116 and 117 make clear that statistically significant testing was performed taking into account variations in sample size and relative gene abundance in different libraries and within each library. Accordingly, the Examiner's basis for this rejection for lack of utility of claims 1-5, 7, 8, 15 because of a questionable tissue source and statistical significance of the identified CLASP2CLASP1 marker is flawed.

The case law on utility is quite clear; mere identification

of a pharmacological activity of a claimed compound that is relevant to an asserted pharmacological use provides an immediate benefit to the public and thus satisfies the utility requirement. Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881, 883 (CCPA 1980). Clearly identification of SEQ ID NO:51 as having detectable expression specific for lung cancer tissue constitutes a pharmacological activity relevant to the asserted use as a diagnostic for lung cancer, thus satisfying the utility requirement with respect to these nucleic acid molecules.

Further, Applicants respectfully disagree with the Examiner's suggestion that the specification is "silent with respect to any potential nucleic acids that fall within claims 1(c) or (d)." Contrary to the Examiner's suggestion the specification provides detailed teachings of nucleic acid molecules meeting the limitations of claim 1(c) and claim 1(d) at pages 31-40. Further, MPEP § 2107.03 and the courts are quite clear, evidence of structural similarity to a compound known to have a particular therapeutic or pharmacological utility is routinely supportive of an assertion of therapeutic utility for the structurally similar compound. Applicants have demonstrated herein the pharmacological utility of SEQ ID NO:51. Further demonstration of utility of structurally similar compounds to SEQ

ID NO:51 such as set forth in parts (c) and (d) of claim 1 is therefore not required.

Withdrawal of these rejections under 35 U.S.C. § 101 and §112, first paragraph, is respectfully requested in light of the claim amendments and the above remarks.

VI. Rejection of Claims 1-5, 7-9 and 15 under 35 U.S.C. § 112, first paragraph - Written Description

Claims 1-5, 7-9 and 15 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

In particular, the Examiner suggests that claims reciting "comprising", "a" nucleic acid of SEQ ID NO:51, "at least 60% sequence identity" or nucleic acids that "selectively hybridize" to a nucleic acid that encodes SEQ ID NO:174 or "a" nucleic acid of SEQ ID NO:51, are inclusive of sequences from other species, mutated sequences, allelic variants, full length genes, genomic DNA, for example, all which have different functions than that of the nucleic acid in SEQ ID NO:51 or the nucleic acid encoding SEQ ID NO:174, while the specification only teaches SEQ ID NO:51.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 1 to clarify that the nucleic acid molecule is lung specific and detectably expressed

in lung cancer tissue, thus clarifying that the nucleic acid molecules have a similar function. Support for this amendment is provided in the specification for example in Example 1. Further, Applicants have amended part (c) of claim 1 to specify conditions of selective hybridization as taught at page 14-16 of the specification. Further, Applicants have amended part (d) of claim 1 in accordance with teachings at pages 32-33 of the specification to state that the nucleic acid molecule has at least 96% sequence identity over at least 200 nucleotides of the nucleic acid molecule encoding SEQ ID NO:174 or SEQ ID NO:51.

Further, Applicants respectfully direct the Examiner to pages 13-16 and Example 1 of the specification wherein detailed methodologies for ascertaining sequences which meet the structural and functional limitations of the instant amended claims are set forth. It is respectfully pointed out that such methods for assessing percent sequence identity and/or the ability of a nucleic acid sequence to hybridize under stringent conditions to a disclosed reference sequence are also performed routinely by those skilled in the art. Thus, upon discovery of the instant claimed nucleic acid sequence of SEQ ID NO:51 and its lung tissue specificity and lung cancer tissue specificity, Applicants were clearly in possession of additional nucleic acid

sequences identified in accordance with routine procedures based upon these reference sequences. Further, the instant specification and its teachings clearly place the public in possession of these sequences as well.

Thus, the instant specification and the claims as amended meet the "essential goal" of the written description requirements of 35 U.S.C. § 112, first paragraph as set forth in MPEP § 2163.

Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, is therefore respectfully requested.

VII. Rejection of Claims 1-2 and 4-5 under 35 U.S.C. § 102(a)

Claims 1-2 and 4-5 have been rejected under 35 U.S.C. § 102(a), 102(b) or (102(f) as being anticipated by LIFESEQ™ Database. The Examiner suggests that "the specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO:51) were procured from, and thereby known by Incyte Genomics Inc. at the time the invention was made." Thus, the Examiner suggests that the nucleic acids of the present invention were known and used in the art prior to the filing of the instant application, were in public use and on sale in this country prior to filing the instant application. Further, the Examiner suggests that this statement is indicative of the sequence being known by Incyte Genomics at the time the invention

was made and therefore not invented by Applicants.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner's characterization of the teachings of the specification at page 116. Contrary to the Examiner's suggestion, no where do Applicants "state" in the instant patent application that "the nucleic acids of the present invention were procured from, and thereby known by Incyte Genomics Inc. at the time the invention was made". Instead, what is taught in Example 1 beginning at page 116 of the instant specification are the steps utilized by Applicants, not Incyte Genomics Inc. to identify the lung cancer specific nucleic acid molecules of the present invention. As clearly stated in this Example, Applicants utilized their own set of algorithms referred to as CLASP™ to systematically interrogate and analyze gene expression data in the LIFESEQ Gold database. It is only by this systematic analysis wherein CLASP categorizes ESTs and genes by disease class and performs simultaneous parallel searching for ESTs and genes expressed selectively in defined tissue types and cancer disease states that the lung specific nucleic acid molecule of SEQ ID NO:51, encoding SEQ ID NO: 174 was identified.

But for applicants proprietary CLASP™ algorithms and the

disclosure of the subject application, one of skill in the art would not know that the claimed lung cancer specific nucleic acids including SEQ ID NO:51 are lung specific or cancer specific, much less lung cancer specific.

In an earnest effort to clearly distinguish the present invention from expression data in the LIFESEQ Gold database, Applicants have amended claim to clarify that the isolated nucleic acid molecules are lung cancer specific. Support for this amendment is provided in Example 1 beginning at 116 wherein Applicants describe use of their CLASP™ algorithms to analyze and identify SEQ ID NO:51 as having CLASP2, meaning detectable expression only in cancer tissue, profiles, and CLASP 1, meaning lung tissue-specific expression.

While sequences or portions thereof may have been in the LIFESEQ database, the Examiner has not shown that the claimed lung cancer specific nucleic acids including SEQ ID NO:51 are disclosed. Accordingly, the LIFESEQ database cannot anticipate the claims as amended.

Withdrawal of these rejections under 35 U.S.C. § 102(a), 102(b) and 102(f) is therefore respectfully requested.

VIII. Rejection of Claims 1-2 and 4-5 under 35 U.S.C. § 102(a)

Claims 1-2 and 4-5 have been rejected under 35 U.S.C. §

102(a) as being anticipated by Birren et al. (GenEmbl Accession No. AC032035). The Examiner suggests that Birren et al. teaches a sequence which is 41.4% identical to Applicants' SEQ ID NO:51 and has best local similarity of 95.1% identity. Thus, the Examiner suggests that since the claims encompass nucleic acids comprising "a" nucleic acid of SEQ ID NO:51 which includes portions of SEQ ID NO:51 of any length, Birren et al. anticipates the claim. The Examiner also suggests that the nucleic acid of Birren et al. would selectively hybridize to SEQ ID NO:51. Further, the Examiner suggests that Birren et al. teaches the nucleic acid is from a cDNA and the nucleic acid is mammalian.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully disagree with the Examiner's suggestion that by the phrase "a nucleic acid of SEQ ID NO:51" it is meant to include portions of SEQ ID NO:51 of any length. Applicants used the term "a" for antecedent basis reasons as this is the first time the nucleic acid of SEQ ID NO:51 was referred to in the claim.

In an earnest effort to advance the prosecution of this case, however, Applicants have amended claim to remove the phrase "a nucleic acid molecule of SEQ ID NO:51" instead merely stating that the nucleic acid molecule comprises SEQ ID NO:51. Thus,

claim 1 as amended is drawn to an isolated lung cancer specific nucleic acid molecule comprising (a) a nucleic acid sequence encoding SEQ ID NO: 174; (b) SEQ ID NO: 51; (c) a nucleic acid molecule that selectively hybridizes under stringent hybridization conditions of 50% formamide/6X SSC at 42°C for at least 10 hours or 6X SSC at 68°C without formamide for at least 10 hours to the nucleic acid molecule of (a) or (b); or (d) a nucleic acid molecule having at least 96% sequence identity over at least 200 nucleotides of the nucleic acid molecule of (a) or (b).

Birren et al. does not teach nucleic acid sequences meeting the limitations of these claims and thus cannot anticipate the claims as amended.

Withdrawal of this rejection is therefore respectfully requested.

IX. Rejection of Claim 15 under 35 U.S.C. § 102(b)

Claim 15 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Mullis et al. (U.S. Patent 4,800,159). The Examiner suggests that Mullis et al. teach a kit comprising a means for determining the presence of the nucleic acid of claim 1 in a sample of a patient.

Applicants respectfully traverse this rejection.

MPEP §2131 is quite clear; to anticipate a claim the reference must teach all the elements of the claimed invention. Claim 15 is drawn to a kit for detecting a risk of cancer or presence of cancer in a patient. The kit comprises a means for determining the presence of a nucleic acid molecule comprising a nucleic acid sequence encoding SEQ ID NO:174; comprising SEQ ID NO:51; selectively hybridizing under defined stringent conditions to a nucleic acid sequence encoding SEQ ID NO:174 or SEQ ID NO:51; or a nucleic acid molecule having at least 96% sequence identity over at least 200 nucleotides of nucleic acid molecule to a nucleic acid sequence encoding SEQ ID NO:174 or SEQ ID NO:51. The general teachings of the Mullis regarding a process for amplifying, detecting and/or cloning nucleic acid sequences in no way teaches a means for detection of these specific nucleic acid molecules.

Thus, withdrawal of this rejection under 35 U.S.C. § 102(b) is respectfully requested.

X. Rejection of Claims 7-9 under 35 U.S.C. § 103(a)

Claims 7-9 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Incyte Genomics LIFESEQ Database, as applied to claims 1-2 and 4-5 supra, and further in view of Prendergast (U.S. Patent 5,958,753). The Examiner suggests that

it would have been obvious to one of ordinary skill in the art at the time the invention was made to have linked the polynucleotides of the LIFESEQ database into expression vectors to have transformed host cells with the resulting vectors and to have used the transformed cells to express polypeptides in order to have provided an effective means for synthesizing polypeptides encoded by the isolated polynucleotides in light of the teachings of Prendergast.

Applicants respectfully traverse this rejection.

At the outset, as discussed in Section VII, supra, Applicants respectfully disagree with the Examiner's characterization of the teachings of the specification which are reiterated in this rejection. Contrary to the Examiner's suggestion, no where do Applicants "state" in the instant patent application that "the nucleic acids of the present invention were procured from, and thereby known by Incyte Genomics Inc. at the time the invention was made".

As made clear in the teachings of the Example 1 beginning at page 116, Applicants, using their CLASP algorithms identified the lung cancer specific nucleic acid molecules of the present invention.

Thus, it is only with the instant specification in hand, and

not merely sequence and expression data as set forth in the LIFESEQ database, that one of skill would be motivated to link the claimed lung cancer specific nucleic acid molecules into vectors and express such vector in host cells.

Accordingly, the combination of cited references provides neither the requisite motivation to combine their teachings nor a teaching of all claim limitations of the claims, now amended to clarify that the isolated nucleic acid molecules are lung cancer specific, to render the instant invention prima facie obvious. See MPEP § 2143.

Thus, withdrawal of this rejection under 35 U.S.C. § 103 (a) is respectfully requested.

Claims 7-9 have also been rejected under 35 U.S.C. § 103(a) as being unpatentable over Birren et al., as applied to claims 1-2 and 4-5, supra, and further in view of Prendergast (U.S. Patent 5,958,753). The Examiner suggests that Prendergast teaches operably linking a polynucleotide into an expression vector, transforming a host cell with the resulting recombinant vector and expressing the polypeptide encoded by the polynucleotide using the transformed host cells.

Applicants respectfully traverse this rejection.

MPEP § 2143.03 and the courts are quite clear; if an

independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

As discussed in detail in Section VIII, supra, Birren et al. does not teach the nucleic acid molecules as set forth in amended claim 1. Accordingly, the primary reference of this 103 rejection fails to teach or suggest all the limitations of the claimed invention.

The teachings of Prendergast fail to remedy this deficiency as this reference is unrelated to lung cancer specific nucleic acid molecules.

Thus, this combination of references cannot render obvious the instant claimed invention as it does not teach or suggest all the limitations of the claimed invention. See MPEP § 2143.

Withdrawal of this rejection under 35 U.S.C. § 103 is therefore respectfully requested.

XI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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